**APPENDIX A**

| Claim | Support Includes |
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| 1. A process for preparing a vascular endothelial growth factor (VEGF) dimer comprising: | Claims 1 and 35 of parent application 09/575,199<br><br>Paragraphs [0009], [0017], and [0028] from the original specification of current application 10/749,703. |
| providing transformed host bacterial cells, | Claims 35 and 43 of parent application 09/575,199<br><br>Paragraphs [0029], [0030], and [0085] from the original specification of current application 10/749,703 |
| wherein the transformed host bacterial cells comprise an exogenous nucleic acid encoding an amino acid sequence of a VEGF monomer operably linked to a promoter, | Claims 35 and 43 of parent application 09/575,199<br><br>Paragraphs [0029] and [0133] from the original specification of current application 10/749,703 |
| wherein the amino acid sequence has at least about 90% sequence identity with amino acids 11 to 116 of SEQ ID NO: 1 | Claims 1, 14, 28, 35, and 54 of parent application 09/575,199<br><br>Paragraph [0028] from the original specification of current application 10/749,703 |
| and wherein the amino acid sequence is extended by a Met-$(AA)_n$- sequence at the amino terminus (N-terminus), | Claims 45, 54, and 65 of parent application 09/575,199<br><br>Paragraphs [0029] and [0033] from the original specification of current application 10/749,703 |
| wherein Met stands for methionine, n is 1-7, and AA represents identical or different amino acids, | Claims 45, 54, and 65 of parent application 09/575,199<br><br>Paragraphs [0029] and [0033] from the original specification of current application 10/749,703 |
| where at least one of the AA amino acids, or a combination of two or more of the AA amino acids, is capable of retarding proteolytic | Claims 45, 54, and 65 of parent application 09/575,199<br><br>Paragraphs [0029] and [0033] from the original specification of current application |

| Claim | Support Includes |
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| degradation of the mature N-terminus of the VEGF dimer by the bacterial host cell, | 10/749,703 |
| and the amino acid sequence retains a cysteine (Cys) at or corresponding to position 116 of SEQ ID NO: 1 (Cys-116); | Claims 1, 14, 28, 35, and 54 of parent application 09/575,199<br><br>Paragraphs [0009], [0011], and [0013] from the original specification of current application 10/749,703 |
| culturing said host cells under conditions suitable for expression of said VEGF monomer, whereby a first VEGF monomer and a second VEGF monomer are produced; | Claim 35 and 54 of parent application 09/575,199<br><br>Paragraphs [0024] and [0030] from the original specification of current application 10/749,703 |
| forming the VEGF dimer from the first and second VEGF monomers; | Claims 1, 14, 28, and 54 of parent application 09/575,199<br><br>Paragraph [0028] from the original specification of current application 10/749,703 |
| and<br>recovering said VEGF dimer. | Claims 35 and 54 of parent application 09/575,199<br><br>Paragraphs [0031] and [0094] from the original specification of current application 10/749,703 |
| 2. The process of claim 1, wherein n is 1. | Claims 46 and 55 of parent application 09/575,199<br><br>Paragraph [0027] from the original specification of current application 10/749,703 |
| 3. The process of claim 2, wherein AA represents an amino acid selected from the group consisting of lysine (Lys) and arginine (Arg) residues. | Claims 47 and 56 of parent application 09/575,199<br><br>Paragraph [0146] from the original specification of current application 10/749,703 |
| 4. The process of claim 3, wherein AA represents a lysine (Lys) residue. | Claims 48 and 57 of parent application 09/575,199<br><br>Paragraph [0146] from the original |

| Claim | Support Includes |
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| | specification of current application 10/749,703 |
| 5. The process of claim 1, further comprising the step of purifying said VEGF dimers. | Claims 42 and 49 of parent application 09/575,199<br><br>Paragraph [0093] from the original specification of current application 10/749,703 |
| 6. The process of claim 5, further comprising the removal of the N-terminal $Met(AA)_n$- sequence following at least partial purification. | Claims 50 and 59 of parent application 09/575,199<br><br>Paragraphs [0077] and [0094] from the original specification of current application 10/749,703 |
| 7. The process of claim 6, wherein removal is performed by enzymatic digestion. | Claims 51 and 60 of parent application 09/575,199<br><br>Paragraphs [0077] and [0094] from the original specification of current application 10/749,703 |
| 8. The process of claim 7, wherein diaminopeptidase is used to perform the enzymatic digestion. | Claims 51 and 60 of parent application 09/575,199<br><br>Paragraph [0094] from the original specification of current application 10/749,703 |
| 9. The process of claim 1, wherein at least about 95% of said VEGF dimers are devoid of an N-terminal methionine residue. | Paragraph [0140] from the original specification of current application 10/749,703 |
| 10. The process of claim 1, further comprising the step of refolding said VEGF dimers. | Claims 52, 61, 62, and 63 of parent application 09/575,199<br><br>Paragraphs [0093] and [0155] from the original specification of current application 10/749,703 |
| 11. The process of claim 10, wherein refolding is performed in a refolding buffer comprising cysteine and cystine in amounts and in | Claims 53 and 64 of parent application 09/575,199<br><br>Paragraphs [0093] and [0155] from the |

| Claim | Support Includes |
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| a ratio to each other sufficient to produce the desired mixture of VEGF dimers. | original specification of current application 10/749,703 |
| 12. A process for producing a vascular endothelial growth factor (VEGF) dimer composed of two VEGF monomers, | Claims 1, 14, 28, and 54 of parent application 09/575,199<br><br>Paragraph [0028] from the original specification of current application 10/749,703 |
| in which each monomer comprises amino acids 11 to 116 of SEQ ID NO: 1, | Claims 1, 14, 28, 35, and 54 of parent application 09/575,199<br><br>Paragraphs [0010], [0011], and [0018] from the original specification of current application 10/749,703 |
| or comprises an amino acid sequence having at least about 90% sequence identity with amino acids 11 to 116 of SEQ ID NO: 1, | Claims 1, 14, 28, 35, and 54 of parent application 09/575,199<br><br>Paragraph [0028] from the original specification of current application 10/749,703 |
| and retaining a cysteine (Cys) at a position corresponding to position 116 of SEQ ID NO: 1 (Cys-116), | Claims 1, 14, 28, 35, and 54 of parent application 09/575,199<br><br>Paragraphs [0009], [0011], and [0013] from the original specification of current application 10/749,703 |
| where Cys-116 of each monomer is disulfide bonded to an additional extraneous Cys, comprising the steps of: | Claims 1, 14, 28, 35, and 54 of parent application 09/575,199<br><br>Paragraph [0028] from the original specification of current application 10/749,703 |
| providing transformed bacterial host cells comprising a species of exogenous nucleic acid encoding a promoter operably linked to a polypeptide of SEQ ID NO: 1 extended by a Met-$(AA)_{\underline{n}}$- sequence at the amino terminus (N-terminus), | Claims 45, 54, and 65 of parent application 09/575,199<br><br>Paragraphs [0029] and [0033] from the original specification of current application 10/749,703 |
| wherein Met stands for methionine, n is | Claims 45, 54, and 65 of parent application 09/575,199 |

| Claim | Support Includes |
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| 1-7, and AA represents identical or different amino acids, | Paragraphs [0029] and [0033] from the original specification of current application 10/749,703 |
| wherein at least one of the AA amino acids, or a combination of two or more of the AA amino acids, is capable of blocking the proteolytic degradation of the mature N-terminus of the VEGF polypeptides by the bacterial host cell; | Claims 45, 54, and 65 of parent application 09/575,199<br><br>Paragraphs [0029] and [0033] from the original specification of current application 10/749,703 |

| Claim | Support Includes |
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| culturing said bacterial host cells under conditions suitable for expression of said exogenous nucleic acid and the synthesis of said N-terminally-extended VEGF monomers, | Claims 54 of parent application 09/575,199<br><br>Paragraphs [0024], [0029], [0030] from the original specification of current application 10/749,703 |
| and<br>recovering said VEGF dimer. | Claims 35 and 54 of parent application 09/575,199<br><br>Paragraphs [0031] and [0094] from the original specification of current application 10/749,703 |
| 13. The process of claim 12, wherein n is 1. | Claims 46 and 55 of parent application 09/575,199<br><br>Paragraph [0027] from the original specification of current application 10/749,703 |
| 14. The process of claim 13, wherein AA represents an amino acid selected from the group consisting of lysine (Lys) and arginine (Arg) residues. | Claims 47 and 56 of parent application 09/575,199<br><br>Paragraph [0146] from the original specification of current application 10/749,703 |
| 15. The process of claim 14, wherein AA represents a lysine (Lys) residue. | Claims 48 and 57 of parent application 09/575,199<br><br>Paragraph [0146] from the original specification of current application 10/749,703 |
| 16. The process of claim 12, further comprising the step of purifying said VEGF dimer. | Claims 42 and 49 of parent application 09/575,199<br><br>Paragraph [0093] from the original specification of current application 10/749,703 |
| 17. The process of claim 16, further comprising the removal of the N-terminal $Met(AA)_n$- sequence following at least partial purification. | Claims 50 and 59 of parent application 09/575,199<br><br>Paragraphs [0077] and [0094] from the original specification of current application 10/749,703 |
| 18. The process of claim 17, wherein | Claims 51 and 60 of parent application 09/575,199 |

| Claim | Support Includes |
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| removal is performed by enzymatic digestion. | Paragraphs [0077] and [0094] from the original specification of current application 10/749,703 |
| 19. The process of claim 18, wherein at least about 95% of said VEGF dimers are devoid of an N-terminal methionine residue. | Claims 51 and 60 of parent application 09/575,199<br><br>Paragraphs [0077], [0094], and [0140] from the original specification of current application 10/749,703 |
| 20. The process of claim 12, additionally comprising the step of refolding said VEGF dimer. | Claims 52, 61, 62, and 63 of parent application 09/575,199<br><br>Paragraphs [0093] and [0155] from the original specification of current application 10/749,703 |
| 21. The process of claim 14, additionally comprising the step of refolding said VEGF dimer. | Claims 52, 61, 62, and 63 of parent application 09/575,199<br><br>Paragraphs [0093] and [0155] from the original specification of current application 10/749,703 |
| 22. The process of claim 17, additionally comprising the step of refolding said VEGF dimer. | Claims 52, 61, 62, and 63 of parent application 09/575,199<br><br>Paragraphs [0093] and [0155] from the original specification of current application 10/749,703 |
| 23. The process of claim 22, wherein refolding is performed in a refolding buffer comprising cysteine and cystine. | Claims 53 and 64 of parent application 09/575,199<br><br>Paragraphs [0093] and [0155] from the original specification of current application 10/749,703 |
| 24. A process for preparing a vascular endothelial growth factor (VEGF) dimer comprising: | Claims 1 and 35 of parent application 09/575,199<br><br>Paragraphs [0009], [0017], and [0028] from the original specification of current application 10/749,703. |
| providing host cells, | Claims 35 and 43 of parent application 09/575,199 |

| Claim | Support Includes |
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| | Paragraphs [0029], [0030], and [0085] from the original specification of current application 10/749,703 |
| wherein the host cells comprise an exogenous nucleic acid encoding an amino acid sequence of a VEGF monomer operably linked to a promoter, | Claims 35 and 43 of parent application 09/575,199<br><br>Paragraphs [0029] and [0133] from the original specification of current application 10/749,703 |
| wherein the amino acid sequence has at least about 90% sequence identity with amino acids 11 to 116 of SEQ ID NO: 1, | Claims 1, 14, 28, 35, and 54 of parent application 09/575,199<br><br>Paragraph [0028] from the original specification of current application 10/749,703 |
| retains a cysteine (Cys) at or corresponding to position 116 of SEQ ID NO: 1 (Cys-116), | Claims 1, 14, 28, 35, and 54 of parent application 09/575,199<br><br>Paragraphs [0009], [0011], and [0013] from the original specification of current application 10/749,703 |
| and wherein at least one monomer has an Asn-to-Glu amino acid substitution at or corresponding to position 75 of SEQ ID NO: 1; | Paragraph [0162] from the original specification of current application 10/749,703 |
| culturing said host cells under conditions suitable for expression of said VEGF monomer, whereby a first VEGF monomer and a second VEGF monomer are produced; | Claim 35 and 54 of parent application 09/575,199<br><br>Paragraphs [0024] and [0030] from the original specification of current application 10/749,703 |

| Claim | Support Includes |
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| forming the VEGF dimer from the first and second VEGF monomers; | Claims 1, 14, 28, and 54 of parent application 09/575,199<br><br>Paragraph [0028] from the original specification of current application 10/749,703 |
| and<br>recovering said VEGF dimer. | Claims 35 and 54 of parent application 09/575,199<br><br>Paragraphs [0031] and [0094] from the original specification of current application 10/749,703 |
| 25. The process of claim 24, wherein each monomer comprises amino acids 1 to 120 of SEQ ID NO: 1. | Claims 6 and 19 of parent application 09/575,199<br><br>Paragraph [0016] from the original specification of current application 10/749,703 |
| 26. The process of claim 24, wherein monomer comprises amino acids 1 to 121 of SEQ ID NO: 1. | Claims 7, 20, 30, 37, and 40 of parent application 09/575,199<br><br>Paragraphs [0035] and [0036] from the original specification of current application 10/749,703 |
| 27. The process of claim 24, wherein at least about 95% of said VEGF dimers are devoid of an N-terminal methionine residue. | Paragraph [0140] from the original specification of current application 10/749,703 |
| 28. The process of claim 24, wherein the Cys residue corresponding to Cys-116 of SEQ ID NO:1 of each monomer is disulfide bonded to an extraneous Cys. | Claims 1, 14, 28, 35, and 54 of parent application 09/575,199<br><br>Paragraph [0028] from the original specification of current application 10/749,703 |
| 29. The process of claim 24, wherein the Cys residue corresponding to Cys-116 of SEQ ID NO:1 of the two monomers are interconnected with an interchain disulfide bond. | Claims 26, 28, and 35 of parent application 09/575,199<br><br>Paragraph [0039] and Figure 4 from the original specification of current application 10/749,703 |
| 30. The process of claim 24, wherein the Cys residue corresponding to Cys-116 of SEQ | Claims 28 and 35 of parent application 09/575,199<br><br>Paragraphs [0045], [0155], [0178], [0179], |

| Claim | Support Includes |
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| ID NO:1 of one or both monomers is not reduced. | [0180] from the original specification of current application 10/749,703 |
| 31. The process of claim 24, additionally comprising the step of purifying said dimers. | Claims 42 and 49 of parent application 09/575,199<br><br>Paragraph [0093] from the original specification of current application 10/749,703 |
| 32. The process of claim 24, wherein said transformed host cells are bacterial cells. | Claims 43, 54, and 65 of parent application 09/575,199<br><br>Paragraph [0085] from the original specification of current application 10/749,703 |
| 33. The process of claim 32, wherein said bacterial cells are *E. coli* cells. | Claim 44 of parent application 09/575,199<br><br>Paragraph [0085] from the original specification of current application 10/749,703 |
| 34. The process of claim 32, wherein the exogenous nucleic acid encodes a polypeptide of SEQ ID NO: 1 extended by a Met-$(AA)_n$-sequence at the amino terminus (N-terminus), | Claims 45, 54, and 65 of parent application 09/575,199<br><br>Paragraphs [0029] and [0033] from the original specification of current application 10/749,703 |
| wherein Met stands for methionine, n is 1-7, and AA represents identical or different amino acids, | Claims 45, 54, and 65 of parent application 09/575,199<br><br>Paragraphs [0029] and [0033] from the original specification of current application 10/749,703 |
| where at least one of the AA amino acids, or a combination of two or more of the AA amino acids, is capable of retarding proteolytic degradation of the mature N-terminus of the VEGF dimer by the bacterial host cell. | Claims 45, 54, and 65 of parent application 09/575,199<br><br>Paragraphs [0029] and [0033] from the original specification of current application 10/749,703 |
| 35. The process of claim 34, wherein n | Claims 46 and 55 of parent application 09/575,199<br><br>Paragraph [0027] from the original |

| Claim | Support Includes |
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| is 1. | specification of current application 10/749,703 |
| 36. The process of claim 35, wherein AA represents an amino acid selected from the group consisting of lysine (Lys) and arginine (Arg) residues. | Claims 47 and 56 of parent application 09/575,199<br><br>Paragraph [0146] from the original specification of current application 10/749,703 |
| 37. The process of claim 36, wherein AA represents a lysine (Lys) residue. | Claims 48 and 57 of parent application 09/575,199<br><br>Paragraph [0146] from the original specification of current application 10/749,703 |
| 38. The process of claim 34, further comprising the step of purifying said VEGF dimers. | Claims 42 and 49 of parent application 09/575,199<br><br>Paragraph [0093] from the original specification of current application 10/749,703 |
| 39. The process of claim 38, further comprising the removal of the N-terminal $Met(AA)_n$- sequence following at least partial purification. | Claims 50 and 59 of parent application 09/575,199<br><br>Paragraphs [0077] and [0094] from the original specification of current application 10/749,703 |
| 40. The process of claim 39, wherein removal is performed by enzymatic digestion. | Claims 51 and 60 of parent application 09/575,199<br><br>Paragraphs [0077] and [0094] from the original specification of current application 10/749,703 |
| 41. The process of claim 32, further comprising the step of refolding said VEGF dimers. | Claims 52, 61, 62, and 63 of parent application 09/575,199<br><br>Paragraphs [0093] and [0155] from the original specification of current application 10/749,703 |
| 42. The process of claim 41, wherein | Claims 53 and 64 of parent application 09/575,199 |

| Claim | Support Includes |
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| refolding is performed in a refolding buffer comprising cysteine and cystine in amounts and in a ratio to each other sufficient to produce the desired mixture of VEGF dimers. | Paragraphs [0093] and [0155] from the original specification of current application 10/749,703 |